49. The compound of Claim 48, wherein said compound is a nucleic acid sequence.

50. The compound of Claim 49, wherein said nucleic acid sequence is an antisense oligonucleotide complementary to a PBR RNA or DNA.

51. The compound of Claim 49, wherein said nucleic acid sequence is contained in a vector.

52. The compound of Claim 49, wherein said nucleic acid sequence is capable of homologously recombining with a PBR DNA.

REMARKS

Entry of the foregoing amendments, reconsideration and reexamination of the subject application, as amended, pursuant to and consistent with 37 C.F.R. §1.112, and in light of the remarks which follow, are respectfully requested.

By the present amendments, Claims 1 to 47 have been cancelled in favor of new Claims 48 through 52 in order to expedite prosecution. All of the newly-submitted claims correspond to the elected invention.

Turning now to the Office Action, Applicants acknowledge their previous Election, with traverse, of Group I, which was directed to compounds which reduce or inhibit expression of peripheral-type benzodiazepine receptor (PBR). As all of Claims 44 through 48 correspond to this Group, all of the claims should be examined in the next Office Action.

The objection to the Sequence Listing is noted. Applicants hereby aver that the substitute paper and computer readable form of the Sequence Listing are the same. Withdrawal of this objection is respectfully requested.

Claims 20, 37 and 39 were rejected under 33 U.S.C. §112, second paragraph, as assertedly being indefinite. This rejection should be moot as the current claims do not abbreviate this term.

Claims 1, 4, 20, 37, 39 and 43 stand rejected under 35 U.S.C. §102(a) as being anticipated by Papadopoulous et al, *JPC*, 272:32129-32135. The Examiner is respectfully advised that this reference is not prior art to the present invention as it constitutes the work of the inventors and was published less than one year prior to the filing of this application. The Examiner is further advised that a Declaration Pursuant to In re Katz will be submitted in order to obviate this rejection.

Claims 1, 4, 20, 37, 39, and 43 also were rejected under 35 U.S.C. §102(b) as assertedly being anticipated by Mosser or Garnier et al. These rejections are addressed together as the issues appear to be the same. Essentially, the position of the Examiner is

that these references teach an antagonist of a peripheral-type benzodiazepine receptor which would read on the prior claims. In particular, both Mosser and Garnier et al teach a polypeptide diazepam binding inhibitor (DBI) referred to as Ro 5-4864 which, at high concentration, inhibits Leydig tumor cell growth. The Examiner indicates that such inhibitor would read on the claims herein.

It is anticipated that the §102 rejection will be moot upon entry of the present claims. In particular, both of these references are directed to a naturally-occurring binding inhibitor which is an intracellular protein which is expressed in a variety of species, tissues, and a number of cell lines. Moreover, this protein was originally purified from rat grain by its ability to displace diazepam from the allosteric modulatory sites for gamma-aminobutyric acid (GABA) action on GABA receptors. By contrast, the present claims are directed to a non-naturally occurring compound that reduces or inhibits the expression of peripheral-type benzodiazepine receptor. Therefore, these references at least do not anticipate the claimed invention. Moreover, the references do not render the claimed invention obvious since there is no incentive to produce non-naturally occurring compounds which possess equivalent activity.

Claims 1, 4, 20, 37, 39 and 43 also are rejected under 35 U.S.C. §112, first paragraph, on the basis the claims are not adequately enabled by the teachings of the disclosure. Essentially, the position of the Examiner is that the specification only enables an inhibitor of PBR gene expression which comprises a vector which deletes such gene

by homologous recombination, and thereby reduces metastasis of a rat tumor cell line. The Examiner indicates that the specification does not broadly enable the invention commensurate in scope with the claims.

However, the position of the Examiner is respectfully traversed. The novelty of the invention hinges on the discovery that inhibiting the expression of a particular type receptor, i.e., peripheral-type benzodiazepine is an effective means of therapy since such DNA is over-expressed in certain cells and tissues, especially breast cancer. This is demonstrated based on the results contained in the subject application, especially the Examiner wherein it is clear that inhibition of PBR expression results in reduced proliferation of tumor cells, especially breast cancer tumor cells. Since the specification convincingly demonstrates, by virtue of a homologous recombination experiment, that the expression of this gene correlates to an effective therapy, it would be well within the purview of ordinary skill to design an assay to identify compounds which similarly antagonist the expression of such receptor, and thereby effectively reduce cancer cell proliferation, i.e., those that over-express PBR receptors. For example, it would be well within the purview of ordinary skill to design an antisense nucleic acid sequence based on the sequence of the PBR gene. Moreover, it would further be within the level of ordinary skill to design ribosomes that would cleave sequences comprised in PBR and RNA and thereby similarly inhibit the expression of PBR. In this regard, the Examiner is respectfully requested to consider the patentability of certain claims which are directed

to embodiments wherein the compound which reduces or inhibits expression of PBR is a nucleic acid sequence in particular, or is an oligo complementary to a PBR RNA or DNA. Moreover, the Examiner is respectfully advised that a claim which has been introduced, i.e., Claim 52, which provides that a nucleic acid sequence is capable of homologously recombining with a PBR DNA. It would appear from Applicant's review of the Office Action that the Examiner has at least concluded that this is sufficiently enabled by the teachings of the subject application. In particular, the Examiner indicates in her statement of the §112 enablement rejection that the specification is enabling for an inhibitor of PBR gene expression by homologous recombination which reduces the metastasis of a rat tumor cell line.

Based on the foregoing, a Notice of Allowance is respectfully requested. If the Examiner has any questions in connection with this Reply, she is respectfully requested to contact the undersigned so that prosecution may be expedited.

Respectfully submitted,

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Date: December 15, 1999